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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/171,928	10/05/98	INOMATA	N 001560-336

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EXAMINER	
BORIN, M	
ART UNIT	**PAPER NUMBER**
1631	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/171,288	Applicant(s) Inomata et al.
	Examiner Michael Borin	Group Art Unit 1631

☒ Responsive to communication(s) filed on *Oct 24, 2000*

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6 and 8-21* is/are pending in the application.

Of the above, claim(s) *1-5 and 15-20* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *6, 8-14, and 21* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *8,10*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Claims

1. Amendment filed 10/24/2000 is acknowledged. Claim 7 is canceled. Claims 6,8 are amended. Claim 21 is added. Claims 1-6,8-21 are pending. Claims 1-5, 15-20 remain withdrawn from further consideration as being drawn to a non-elected groups.

Claim Rejections - 35 U.S.C. § 112, second paragraph.

2. Rejection of claim 6-14 under 35 U.S.C. 112, second paragraph, is withdrawn in view of amendments to claim 6.

Claim Rejections - 35 U.S.C. § 102 and 103.

3. Applicant amended claim 6 to limit the claimed method to treatment of cardiac hypertrophy by reducing heart weight by the mechanism not based on diuretic and hypertensive effect. The rejections of record are modified to reflect the amendment to the claim.

4. Claims 6,8-10,21 are rejected under 35 U.S.C. 102(b) as anticipated by Blaine et al. (US Patent 4652549) as evidenced by Espiner[1].

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[1]Note that, although the date of the "Espiner" reference is later than the priority date of the instant application, the reference is a review describing studies preceding the instant application; the reference is used merely to demonstrate well known mechanisms of action.

Blaine teaches method of treatment of cardiac hypertrophy using atrial natriuretic peptide (ANF) and fragments thereof. See abstract, summary, claims 1-8. The referenced method anticipates the instantly claimed method of treatment of heart disease based on hypertrophy comprising administration of a substance that acts on natriuretic receptor, guanylyl cyclase A and is able to accelerate production of cGMP. Note, that it is well known that ANF, as well as its analogs stimulate guanylate cyclase A and production of cGMP. See Espiner, p. 205, last paragraph. Therefore, the effects of ANF as instantly claimed are inherently present.

In regard to claim 7, chronic heart failure is a disease based on cardiac hypertrophy.

In regard to claim 10, Espiner teaches that BNP is a functional equivalent of ANP. See p. 205, right column through p. 206, left column.

Response to arguments

Applicant argues that Blaine's disclosure is (1) limited to demonstration of reduction in water content in heart and (2) that the reference does not teach that a substance which acts on guanylyl cyclase A is effective for reducing heart weight by a mechanism separate from diuretic and hypotensive effect.

The only positive method step claimed is administration of natriuretic factor in the amount effective to treat cardiac hypertrophy. The referenced method is comprises the same method step, even though the particular mechanism as instantly claimed is not addressed in the reference. Note that prior art acknowledges that, first, natriuretic peptides have a wide range of actions, and, second,

hypertrophy is a result of an interaction between a variety of different interrelated signaling pathways. See, for example, Espiner, p. 205, right column, lines 30-33; Hefti, p.2873, summary. Therefore, it is not possible to discern which particular mechanism was engaged in achieving an overall effect of treatment. Even though separate mechanisms might have been demonstrated in specifically designed model conditions, Examiner assumes that the referenced method inherently included the effect as instantly claimed. Since the Office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on applicant to show that the referenced method did not include the effect as instantly claimed.

5. Claims 6,8-10,21 are rejected under 35 U.S.C. 102(b) as anticipated by Neustadt et al. (US Patent 5356925).

Neustadt et al. teach treatment of cardiovascular disorders, such as hypertension, congestive heart failure, renal insufficiency (i.e. diseases based on cardiac hypertrophy) using combination of natriuretic peptide(s) and ACE inhibitor. The referenced method anticipates the instantly claimed method of treatment of heart disease based on hypertrophy comprising administration of a substance that acts on natriuretic receptor, guanylyl cyclase A and is able to accelerate production of cGMP. Note that the claimed language "comprising" is not limited on one active ingredient and thus reads on methods of use of formulations comprising natriuretic peptide. Further note, that it is well known that ANF, as well as its analogs stimulate guanylate cyclase A and production of cGMP. See Espiner, p. 205, last paragraph. Therefore, the effects of ANF as instantly claimed are inherently present.

In regard to claim 10, Espiner teaches that BNP is a functional equivalent of ANP. See p. 205, right column through p. 206, left column.

Response to arguments

As in the discussion of the previous rejection, applicant argues that the referenced method is (1) limited to demonstration of hypertensive effect and (2) that the reference does not teach that a substance which acts on guanylyl cyclase A is effective for reducing heart weight by a mechanism separate from diuretic and hypotensive effect.

The rejection is maintained for the same reasons as set forth in regard to the previous rejection.

6. Claims 6,8,9,21 are rejected under 35 U.S.C. 102(b) as anticipated by Berman et al. (JP 63303998) as evidenced by Espiner[2].

Berman et al. teach treatment of cardiac hypertrophy using atrial natriuretic peptide (ANF) analogues which bind to natriuretic receptor. See abstract. The referenced method anticipates the instantly claimed method of treatment of heart disease based on hypertrophy comprising administration of a substance that acts on natriuretic receptor, guanylyl cyclase A and is able to accelerate production of cGMP. Note, that it is well known that ANF, as well as its analogs

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[2]Note that, although the date of the "Espiner" reference is later than the priority date of the instant application, the reference is a review describing studies preceding the instant application; the reference is used merely to demonstrate well known mechanisms of action.

stimulate guanylate cyclase A and production of cGMP. See Espiner, p. 205, last paragraph. Therefore, the effects of ANF analogues as instantly claimed are inherently present.

Response to arguments

Applicant argues that "there is nothing in the reference to show that the peptide analogues can be used to effectively treat cardiac hypertrophy". Applicant's attention is directed to the English language abstract (supplied by the applicant), second line from the bottom.

Further, applicant argues, as in regard to the previous rejections that the reference does not teach that ANP is effective for reducing heart weight by a mechanism separate from diuretic and hypotensive effect.

The rejection is maintained for the same reasons as set forth in regard to the previous rejections.

7. Claims 6,11-14 remain rejected under 35 U.S.C. 103(a) as obvious over Blaine or Berman or Neustadt. The references are applied as above.

If there are any differences between Applicant's claimed methods and that of the prior art, the differences would be appear minor in nature. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal ways of administration and pharmaceutical carriers as they are art-recognized result-effective variable which would have been routinely determined and optimized in the pharmaceutical art.

Note that previous rejections have been maintained.

8. Claims 6,8-14,21 are rejected under 35 U.S.C. 103(a) as obvious over Blaine or Berman or Neustadt in view of Cao et al. (Hypertension, 25, 227-234, 1995; the reference is cited in the specification, p.8).

The primary references (as discussed above) teach treatment of cardiac hypertrophy by natriuretic peptides. The primary references do not specifically teach that the effect achieved as a result of the treatment include reduction of heart weight by a mechanism not based on diuretic or hypotensive effect.

Cao et al teaches that (1) Cardiac hypertrophy include stimulation of gene cascade; (2) natriuretic peptides reduce stimulation of this cascade, as evidenced by a decrease in thymidine incorporation. Thus, the reference suggests that "such growth-suppressing activity raise the intriguing possibility that [natriuretic peptides] may function in paracrine fashion to modulate growth in the interstitial compartment during cardiac hypertrophy. See p. 227, bottom. (3) Demonstrates that the hypertrophy-reducing effect of the natriuretic peptides is due to their interaction with guanylyl cyclase A natriuretic peptide receptor and is further mediated by formation of cGMP (p. 231, and p. 233, second paragraph.

Therefore, it would be obvious to one skilled in the art that cardiac hypertrophy can be reduced by natriuretic peptides by interference with gene activation and that the effect of treating cardiac hypertrophy described in the referenced methods might have included the mechanism as instantly claimed.

Conclusion.

9. No claims are allowed

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael

Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MICHAEL BORIN, PH.D
PATENT EXAMINER

Michael Borin
Primary Examiner
AU1631